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<b>(21) International Application Number:</b> PCT/GB95/02284 <b>(22) International Filing Date:</b> 26 September 1995 (26.09.95)  <b>(30) Priority Data:</b> 9419572.4 29 September 1994 (29.09.94) GB 9501514.5 26 January 1995 (26.01.95) GB 9516930.6 18 August 1995 (18.08.95) GB  <b>(71) Applicant (for all designated States except US):</b> INNOVATIVE TECHNOLOGIES LIMITED [GB/GB]; Road Three, Winsford Industrial Estate, Winsford, Cheshire CW7 3PD (GB).  <b>(72) Inventors; and</b> <b>(75) Inventors/Applicants (for US only):</b> QIN, Yimin [CN/GB]; 123 Victoria Road, Northwich, Cheshire CW9 5RQ (GB). GILDING, Keith, Dennis [GB/GB]; Nepenthe, Winsford Road, Wettenhall, Winsford, Cheshire CW7 4DL (GB).  <b>(74) Agent:</b> ATKINSON, Peter, Birch, Marks & Clerk, Sussex House, 83-85 Mosley Street, Manchester M2 3LG (GB).		<b>(81) Designated States:</b> AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT, UA, UG, US, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG), ARIPO patent (KE, MW, SD, SZ, UG).  <b>Published</b> <i>With international search report Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
<b>(54) Title:</b> FIBRES  <b>(57) Abstract</b>  Fibres which are useful in wound dressings comprise an alginate co-spun with at least one water soluble organic polymenic species (other than an alginate). Examples of such fibres comprise alginate and CMC.		

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## **FIBRES**

The present invention relates to alginate containing fibres which are useful particularly, but not exclusively, in the manufacture of wound dressings.

Alginates are a family of polymers which may be obtained from seaweed and which contain varying proportions of mannuronic and guluronic residues depending on the source of the polymer.

It is established practice to produce alginate fibres by spinning a solution of a soluble form of an alginate polymer into a gelation (or coagulation) bath in which an insoluble form of the alginate precipitates. Typically the soluble form of the polymer is the sodium salt and the bath contains calcium ions to produce insoluble calcium alginate. Fibres produced in this way have high absorbency and are used in the manufacture of wound dressings, e.g. for wet wounds such as pressure sores, leg ulcers, surgical incisions and donor sites where the primary function of the alginate is to absorb exudate.

The present invention relates to modified alginate fibres which are useful in wound dressings.

According to a first aspect of the present invention there is provided fibres comprising an alginate co-spun with at least one water soluble organic polymeric species (other than an alginate).

According to a second aspect of the invention there is provided a method of producing fibres comprising co-spinning a dope which contains dissolved alginate and

at least one dissolved organic polymeric species (other than an alginate) into an aqueous coagulation bath which causes precipitation of fibres each comprised of the alginate and said other polymeric species.

The non-alginate polymer is preferably (but not necessarily) one having negative charges along the polymer chain, i.e. a polyanion. Alternatively the polymer may be uncharged.

Preferably the fibres comprise 70-95% by weight alginate and 5-30% by weight of the non-alginate polymer.

The incorporation of the water soluble non-alginate polymeric species into the fibres with the alginate allows useful fibres of modified properties to be obtained, as compared to the properties obtained of the alginate is the sole component of the fibres. The modified properties may, for example, be increased absorbency of the fibres.

Generally the fibres will comprise a major proportion by weight of the alginate, e.g. 50-95% by weight, and a minor proportion of the non-alginate polymeric species. The alginate may be one having a G-content of 35-70% and correspondingly an M-content of 65-30% by weight. Typically the alginate will be such that a 1% solution will have a viscosity of 30-300 cP, preferably 40-100 cP.

If the non-alginate polymeric species contains negatively charged groups, these may be provided, for example, by  $\text{COO}^-$  or  $\text{SO}_4^{2-}$  groups along the polymer chain.

In one embodiment of the invention, alginates may be co-spun with non-alginate species containing  $\text{COO}^-$  groups along the chain, examples of which include polysaccharides, polycarboxy amino acids it is also possible to use acrylic acid and/or

methacrylic acid, or salts thereof (e.g. the sodium salt). More specific examples include pectin, carboxymethyl cellulose, N,O-carboxymethyl chitosan (NOCC), carrageenan, xanthan, gellan, polyaspartic acid and polyglutamic acid.

The alginate may be co-spun with a non-alginate polymer containing  $\text{COO}^-$  groups which results in a fibre having increased absorbency as compared to one prepared from the alginate alone. Examples of such non-alginate polymers which result in increased absorbency include carboxymethyl cellulose, carrageenan, polyacrylic acid and NOCC. Thus fibres of improved absorbency may comprise 70-90% alginate and a total of 5-30% of at least one of CMC, carrageenan, polyacrylic acid and N,O-carboxymethyl chitosan (NOCC) or O-carboxymethyl chitosan (OCC).

If the alginate is co-spun with pectin, fibres are produced which, when made into (and used) as a wound dressing, soften dry wounds, start autolysis procedures, and assist debridement macrophage stimulation. Preferably the pectin comprises 5-30% (more preferably 10-20%) by weight of the fibres.

The presence of pectin (which consists chiefly of partially methoxylated polygalacturonic acids) does reduce the absorbency of the fibres. Therefore a balance may need to be struck between the absorbency of the fibres (as provided by the alginate) and the wound healing properties thereof (as provided by the pectin). It is possible to co-spin alginate, pectin and at least one non-alginate polymer bearing negative charges which boosts absorbency. Thus fibres may be produced by co-spinning alginate, pectin and either CMC, NOCC or OCC, typically in a ratio of 60%-80% alginate, 10%-20% pectin and 10%-20% CMC, NOCC or OCC.

Further examples of fibres which may be produced in accordance with the first embodiment of the invention include a mixture of components producing a product which is a cross between an alginate and a hydrocolloid. Thus, for example, it is possible to spin such alginate/hydrocolloid products from solutions of alginate, gelatin, pectin, and CMC, e.g. in the following amounts:

Alginate	Gelatin	Pectin	CMC
45	10	25	20
35	10	35	20

In a second embodiment of the invention, the non-alginate polymeric species is one containing  $\text{SO}_4^{2-}$  groups along the polymer chain. Examples include sulphonated polysaccharides which are naturally occurring elements of tissue (serving to keep water in the tissue). Co-spinning of alginates with sulphated polysaccharides results in materials which may be likened to artificial tissue.

Specific examples of sulphated polysaccharides which may be co-spun with alginate include chondroitin, dermatan, and heparan sulphates as well as heparin. Fibres comprising alginate co-spun with at least one of these polysaccharides provide an ideal matrix for growth of tissue (e.g. skin on a burn).

In a further embodiment of the invention, the non-alginate polymer is uncharged. Examples of such uncharged polymers which may be used include Ace Mannan (e.g. clinical grade material as obtainable from Carrington Laboratories, Dallas, Texas, U.S.A) or other component of Aloe Vera.

As indicated above, the incorporation of the water soluble non-alginate polymeric species produces fibres having modified properties compared to those containing pure alginate. Whilst we do not wish to be bound by any particular theory, we believe this is because pure alginate fibre has a compact "egg box" structure and the non-alginate polymer can disrupt the regular packing of the alginate materials therefore providing increased swelling and absorbency capability. In the case of fibres comprising alginate and 15% CMC, we have found that the absorbency of a non-woven dressing produced therefrom was 19 g/g as compared to 17 g/g for a dressing produced from fibres of the alginate which had not been co-spun with the CMC.

Apart from absorbency changes, the non-alginate component may introduce active healing or other medical properties in the dressing. The inclusion of pectin, for example, increases the debridement properties of the dressing.

Fibres in accordance with the invention may be produced by spinning a dope comprising a total dissolved solids content of less than 10% (e.g. about 6%) into an aqueous medium containing cations which will result in the formation of insoluble fibres. The amount of the cation may, for example, be less than 1% by weight.

In the case of non-alginate polymers containing  $\text{COO}^-$  groups it is preferred that the coagulating cation is calcium. If the non-alginate polymer contains  $\text{SO}_4^{2-}$  groups, it is preferred that the coagulating cation is zinc because of the greater insolubility of the calcium sulphate bridge which will cause slower ion exchange with ions in wound fluids. However this type of slower ion exchange can effectively be used to 'fine-tune' the exudate handling characteristics. This zinc and calcium for instance behave in

opposite ways in sulphated species as compared to carboxylated molecules, i.e. calcium is a more effective cross-link in sulphated molecules whereas zinc is more effective in carboxylated species.

The invention will be illustrated by the following non-limiting Examples.

#### Example 1

This example describes the production of alginate/CMC/pectin fibres.

A spinning dope was prepared by mixing 12 kg of sodium alginate (Protanal LF10/60, (available from Pronova Biopolymers), viscosity in 1% solution between 40 to 60 cps), 1.5 kg of sodium carboxymethyl cellulose and 1.5 kg of high methyloxy pectin in 235 litres of water. After storage at room temperature for two days to remove the bubbles, fibres were produced by extruding the dope through a 40,000 hole spinneret (hole diameter 70  $\mu$ m) at 12 m/min. The as-spun fibres were taken up at 7.2 m/min and then stretched at 80°C to 9 m/min. The fibres were then washed with water before they were dried by first passing the fibres through an acetone bath and then drying with heated air. Finally, the dry tow was crimped and cut to produce staple fibres. The staple fibres could be carded and needled to form a non-woven felt which could be cut into individual dressings.



### Example 2

This example describes the production of alginate/CMC fibres.

Example 1 was repeated except that the dope was produced by mixing 13.5 kg of sodium alginate (Protanal LF10/60, viscosity in 1% solution between 40 to 60 cps) and 1.5 kg of sodium carboxymethyl cellulose in 235 litres of water. The fibres could be spun and carded into a non-woven dressing as in Example 1.

The alginate/CMC dressing as produced in this way had an absorbency of 19 g/g as compared to 17 g/g for dressings made from fibres without addition of CMC under exactly the same processing conditions.

### Example 3

This Example describes the production of alginate/Ace Mannan fibres.

Example 1 was repeated except that the dope was produced by mixing 13.5 kg of sodium alginate (Protanal LF10/60, viscosity in 1% solution between 40 to 60 cps) and 1.5 kg of Ace Mannan (ex-Carrington Laboratories) in 235 litres of water. The fibres could be spun and carded into a non-woven dressing as in Example 1.

### CLAIMS

1. Fibres comprising an alginate co-spun with at least one water soluble organic polymeric species (other than an alginate).
2. Fibres as claimed in claim 1 comprising a major proportion by weight of the alginate.
3. Fibres as claimed in claim 2 comprising 50-95% by weight of alginate.
4. Fibres as claimed in claim 3 comprising 70-95% by weight of alginate and 5-30% by weight of said water soluble organic polymeric species.
5. Fibres as claimed in any one of claims 1 to 4 wherein said water soluble organic polymeric species has negative charges along the polymer chain.
6. Fibres as claimed in claim 5 wherein the negative charges for the non-alginate polymer are provided by COO<sup>-</sup> groups provided along the polymer chain.
7. Fibres as claimed in claim 6 wherein the non-alginate polymer is a polysaccharide, polycarboxy amino acid, polyacrylic acid, polymethacrylic acid or salt of such an acid.

8. Fibres as claimed in claim 7 wherein the non-alginate polymer is pectin, carboxymethyl cellulose, N,O-carboxymethyl chitosan, carrageenan, xanthan, gellan, polyaspartic acid or polyglutamic acid.

9. Fibres as claimed in claim 5 wherein the negative charges in the non-alginate polymer are provided by  $\text{SO}_4^{2-}$  groups.

10. Fibres as claimed in claim 9 wherein the non-alginate polymer is a sulphated polysaccharide.

11. Fibres as claimed in claim 10 wherein the sulphated polysaccharide is chondroitin sulphate, dermatan sulphate, heparan sulphate or heparin.

12. Fibres as claimed in any one of claims 1 to 4 wherein said water soluble organic polymeric species is uncharged.

13. Fibres as claimed in claim 12 wherein said water soluble organic polymeric species is Ace Mannan or other component of Aloe Vera.

14. A wound dressing comprising fibres as claimed in any one of claims 1 to 13.

15. A method of producing fibres comprising co-spinning an aqueous dope which contains dissolved alginate and at least one dissolved organic polymeric species having negative charges along the polymer chain into a coagulation bath which causes precipitation of fibres each comprised of the alginate and said other polymeric species.

## INTERNATIONAL SEARCH REPORT

Internat Application No  
PCT/GB 95/02284

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 6 D01F/04 A61L15/28

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
IPC 6 D01F A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE WPI Section Ch, Week 8705 Derwent Publications Ltd., London, GB; Class B04, AN 87-033299 & JP,A,61 289 886 ( AGENCY OF IND SCI TECH) , 19 December 1986	1-11,14, 15
Y	see abstract	12,13
X	--- EP,A,0 527 271 (KOREA RES INST CHEM TECH) 17 February 1993 see the whole document	1-7,14, 15
P,Y	--- WO,A,95 00184 (CARRINGTON LAB INC) 5 January 1995 see the whole document -----	12,13

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# INTERNATIONAL SEARCH REPORT

Information on patent family members

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP-A-0527271	17-02-93	US-A- 5166231 US-A- 5210117	24-11-92 11-05-93
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